THE ROLE OF CHANCE IN DISCOVERY[1]

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In 1751 Horace Walpole, the English statesman and diplomatist, wrote a letter to his friend, Horace Mann, in which he proposed adding a new word to our vocabulary, "serendipity." The word has not had large usage. It is not commonly found in dictionaries of the English language. When I mentioned "serendipity" to one of my acquaintances and asked him if he knew the meaning, he suggested that it probably designated a mental state combining serenity and stupidity! He was mistaken.

Walpole's proposal was based upon his reading of a fairy tale, entitled "The Three Princes of Serendip." Serendip, I may interject, was the ancient name of Ceylon. "As their Highnesses traveled," so Walpole wrote, "they were always making discoveries, by *accident* or *sagacity*, of things they were not in quest of." When the word is mentioned in dictionaries, therefore, it is said to designate the happy faculty, or luck, of finding unforeseen evidence of one's ideas, or with surprise coming upon new objects or relations which were not being sought. In the progress of man's adjustment to the world in which he lives there have been many instances of serendipity.

Probably the most astounding instance of accidental discovery in history was the finding of the western hemisphere by Columbus. He sailed away from Spain firm in the faith that thus he would learn a shorter route to the East Indies and, quite unexpectedly, he encountered a whole new world. It is noteworthy that he was not at first aware of the significance of what he had found. Indeed, it has been said that he did not know where, in fact, he was going, nor where he was when he arrived, nor where he had been after he returned, but nevertheless he had had one of the most remarkable experiences of all time. The important matter is that he did realize that it was a remarkable experience and followed it by making other voyages and thereby extended his knowledge of what he had done and laid a course which others might follow. Such consequences have been common when accident has been favorable to a seeker after new things and the adventure has been fruitful.

In the records of scientific investigation there are many instances of this sort of happy use of good fortune. Consider for a moment the source and the development of our acquaintance with electrical phenomena. It is reported that some frog legs were hanging by a copper wire suspended from an iron balustrade (note the two different metals, copper and iron) in the Galvani home in Bologna; they were seen to twitch when they swung in the wind and happened to touch the iron. Whether the twitching was first noted by Luigi Galvani, the anatomist and physiologist, or by Lucia Galvani, his talented wife, is not clear. Certainly the accidental occurrence was not neglected, for it was the beginning of a long series of researches by Galvani into the electrical manifestations of living tissues—researches which have preserved Galvani's name in the terms "galvanize" and "galvanism." And it also led to experiments by Volta on the production of electric currents by contact of two dissimilar metals, and thus to the invention of the electric battery—experiments so fundamentally important that Volta's name is retained in the daily use of "volt" and "voltage" in speaking of

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electrical potential. Such was the origin of the telegraph and, indirectly, of the telephone, radio-broadcasting and the promise of practical television. And such also was the origin of our knowledge of animal electricity which we now use to tell the condition of the heart muscle, because every heart beat sends forth an electrical wave in the body of each of us, a wave which has an altered form when the heart is injured; and the animal electricity which we are beginning to use to learn about conditions in the brain, because of the rhythmic electrical pulsations which delicate instruments, applied to the surface of the scalp, can reveal as typical activities of that wonderful organ in various conditions of rest and activity, health and disease.

Even in the growth of electrical science serendipity has played important roles. It was by pure chance that the mysterious relation between electricity and magnetism was discovered. The Danish physicist, Oersted, at the end of a lecture happened to bring a wire, which was conducting a strong current, to a position above and parallel to a poised magnetic needle. Previously, and by intent, he had held the wire perpendicularly above the needle, but nothing happened; now, however, when the wire was set horizontally along the needle's length, he was astonished to note that, without any visible connection, the needle swung around until it was almost at right angles to its former position. With quick insight he reversed the direction of the current in the wire and found that the needle then deviated in the opposite direction. Later, when clearly understanding the situation, Faraday proved not only that an electric current in a wire can move a magnet, but also that a moving magnet can cause a current to appear in a wire. From these trifling and casual incidents has gradually evolved our vast modern electrical industry—its immense generators, its ingenious devices for distributing extensively over great areas the power which provides innumerable conveniences for human service—light in dark places, a cooling breeze on a summer day, heat for our morning toast, sparks in motor cylinders, the automatic management of complex machines, safety at sea, and what not else that is helpful in our daily lives. When we consider the prodigious and intricate involvement of electricity in the affairs of mankind throughout the world, Galvani's frog legs may be regarded almost as important as the caravels of Columbus.

In the biological sciences serendipity has been quite as fruitful as in the physical sciences. May I call your attention to some instances. The eminent French physiologist, Claude Bernard, had the idea that the impulses which pass along nerve fibers set up chemical changes which produce heat. About the middle of the last century he measured the temperature of a rabbit's ear, and then severed the nerve which delivers impulses to that structure, expecting, of course, in accordance with his theory, that the ear, deprived of nerve impulses, would be cooler than its mate on the other side. To his great surprise it was considerably warmer! Without knowing what he had done, he had disconnected the blood vessels of the ear from the nervous influences which normally hold them moderately contracted, and thereupon the warm blood from internal organs flushed through the enlarged vessels in a faster flow. Thus by accident appeared the first intimation that the passage of blood into different parts of the body is under nervous government—the most significant advance in our knowledge of the circulation since Harvey's proof, more than 300 years ago, that the blood does, indeed, circulate.

Another striking instance of accidental discovery has been described by the investigator himself, Charles Richet. It was concerned with that peculiar sensitiveness toward certain things—such as white of egg, strawberries, ragweed pol-

len and numerous others—*anaphylaxis* or *allergy*. It commonly results from an initial exposure to the substance which later becomes poisonous. The phenomenon had been noted incidentally before Richet's time, but because it did not receive attention it was virtually unknown. In his charming little book, "Le Savant," he has told the story of how, quite unexpectedly, he happened upon the curious fact. He was testing on a laboratory animal an extract of the tentacles of a sea anemone in order to learn the toxic dose. When animals which had readily survived that dose were given, after a lapse of some time, a much smaller dose (as little as one tenth the original), he was astounded to find that it was promptly fatal. Richet declares that at first he had great difficulty in believing that the result could be due to anything he had done. Indeed, he testifies that it was in spite of himself that he discovered induced sensitization—that he would never have dreamt that it was possible!

An accident may be the occasion for scientific advances because of the serious problem which it presents. Let me cite a striking example. No one anticipated that the polishing of rice would be harmful. Yet removal of the covering from the kernels resulted in tens of thousands of victims of the disease, beri-beri, and in immeasurable sorrow and distress. As Mathews has pointed out, however, the study of beri-beri, thus unwittingly induced, revealed not only the cause of that disease but started exploration in the whole realm of deficiency diseases as well, and drove investigators to the discovery of some of the most intimate secrets of cellular processes.

A quite recent instance of serendipity was the finding of vitamin K, lack of which deprives the blood of an essential element for its coagulation. Dam and his collaborators in Copenhagen were working on sterol metabolism in chicks. They noted that the animals on the restricted diet often exhibited extensive internal hemorrhages, subcutaneous and intramuscular. When the diet was changed to seeds plus salts, the hemorrhages failed to occur. By critical tests the disease was proved not to be due to lack of any previously known vitamin, but to lack of a specific antihemorrhagic agent, contained in hog liver fat, certain vegetables and in many cereals. This agent, vitamin K, is reported to be an important factor in surgery. Patients afflicted with obstructive jaundice can be relieved by an operation, but unfortunately in that condition their blood may clot very slowly and therefore they are in danger of disastrous bleeding. This danger can now be readily obviated by feeding vitamin K (with bile salts), for it restores to an effective concentration the deficient element of the clotting process—a happy benefit to human beings coming from a chance observation on chicks.

There are many other noteworthy instances of serendipity which I might detail to you; among them Nobel's invention of dynamite, Perkin's stumbling upon the coal-tar dyes and Pasteur's finding that a vegetable mold caused the watery solution which nurtured it to change the light rays as they passed through. Dynamite placed gigantic powers in the hands of man; the coal-tar dyes have fundamentally affected such varied activities as warfare, textile industries and medical diagnosis, and Pasteur's casual observation has developed into an immense range of chemical theory and research.

Three legends of accidental intimations which led to fresh insight will allow me to introduce the next point which I wish to emphasize—the importance of the prepared mind. It is said that Archimedes had the idea of specific gravity suggested to him while noting by chance the buoyancy of his body in water. And we have all heard the tale that Isaac Newton was led to the concept of a universal law of gravitational force when he saw an apple fall from a tree as he lay

musing on the grass in an orchard. Of similar character is the report that the possibility of the steam engine came to the mind of James Watt when he beheld the periodic lifting of a tea-pot lid by the pressure of the water-vapor within the pot. Now, many a man floated in water before Archimedes, apples fell from trees as long ago as the Garden of Eden (exact date uncertain!), and the outrush of steam against resistance could have been noted since the invention of fire. In all three instances a long time passed before the significance of the event was perceived. Obviously, a chance discovery not only involves the phenomenon to be observed, but also the appreciative and intelligent observer.

It was in recognition of this fact that the wise and discerning dictum of Pasteur is displayed in prominent letters in the corridor of the students' dormitory of the Harvard Medical School—"Dans les champs de l'observation le hazard ne favorise que les esprits préparés." In the fields of observation chance favors only the minds which are prepared. That expression has important implications.

In the course of our human experience no one can tell what new circumstances may arise, nor can one predict the moment of their arrival. To-morrow opportunities may appear the seizure of which or the neglect of which may have long-lasting and fateful consequences. There is a tide in the affairs of all of us which "taken at its flood leads on to fortune"—and not taken may lead on to misfortune. In other words, the unexpected is continually happening in our lives, much as it happens in the realms of exploration and scientific research. Chance throws peculiar conditions in our way and, if we have alert and acute vision, we see their importance and use the opportunity which chance provides.

What are the prerequisites favorable for making greatest use of a novel occasion when it arrives?

First of all, if we are to benefit by such an occasion for securing fresh insight and enlarging our experiences in untried directions we must be well equipped with knowledge of the past. Only when we know what has already been done by others who have gone before us can we judge the present scene. The word "research" is commonly employed to indicate scientific investigation. Why is not the word "search" quite as exact? The "re" in "research" implies that the investigator studies carefully the methods and results of earlier investigators and *looks again* at the problems which they strove to solve, with the advantage now of possessing all accumulated previous knowledge, ready for the flashing of an illuminating idea. That is the method of discovery in its most elaborate development. We do not need to go to such lengths, however, in order to enjoy in a mild way the satisfaction of bringing to bear, in unanticipated circumstances, the stored memories of bygone events. A historical reference in speech or literature, or a name in a poem, is endowed with larger significance if we contribute to it rich associations from our own past. "In Xanadu did Kubla Khan a stately pleasure-dome decree" are lines which do not demand information in order to appreciate their musical beauty, but if one knows the story of Kubla Khan as the poet knew it, and is acquainted with oriental magnificence, the words take on an enlarged and special meaning. Furthermore, with the mind prepared there is always the favoring possibility of continuing enrichment as one grows older. One brings to the reading of history and literature, to the unpredictable incidents of travel, to the flashing moments of conversation, and to the varied adventures of the passing years a substantial basis on which can be gradually developed manifold interests and the happy relations of the individual to his fellows and to his surroundings.

In the life of every investigator who

has had much experience, occasions of happy chance are likely to be found. During the past four decades in my own labors instances of such good fortune have several times occurred. When a man has passed his sixtieth year, it is said, he may at last be permitted, without censure, to engage in reminiscence. Perhaps you will be tolerant, therefore, if I recount to you an example of serendipity that fell to my lot. After all, an investigator is not taking undue credit to himself when he calls attention to the fact that results which he has obtained in his researches have depended on a fortuitous incident and not on his own intelligence and insight! Of course, the case which I shall cite is not to be compared with the great discoveries of Bernard, Richet and Pasteur, but it will illustrate equally well some of the conditions which prevail when chance plays a role in discovery.

About forty-three years ago, shortly after the x-rays were discovered, I was using the mysteriously penetrating light to look into animals in order to watch the little known processes of digestion. The churning and mixing of the food was clearly visible. Occasionally, however, my purposes were wholly checked because the motions came to a dead stop. That was a great annoyance; it seemed very strange, and I was at a loss to account for it. But in scientific investigations, as in daily living, obstacles may yield important values. I soon noticed that the cessation of the digestive activities was associated with signs of anxiety or other emotional disturbance. Could it be that I was seeing the harmful effects of worry on the organs which serve to make the food useful to the body? That proved to be true, for when I petted the animals reassuringly the churning waves promptly started again, and when excitement was induced the waves promptly stopped. There was an instance of serendipity—a discovery which I was "not in quest of," a disclosure which called for the application of "sagacity," to use Horace Walpole's expressions. It was the beginning of many years of research on the influence of fear and rage on bodily functions—research which ultimately led to insight into the agencies of our organism which maintain the stability of the extraordinarily unstable material of which we are composed and which give us freedom to live and carry on our various activities untrammeled by external heat or cold, by flight to high altitudes or by the internal changes produced by strenuous efforts in which we may engage. The observation of the effects of worry on digestion also resulted ultimately in a suggestive concept of the nature of emotional excitement, and, furthermore, in the demonstration of a chemical agent which acts as an intermediary between nerves and muscles when muscles are made to contract or relax.

There is another implication in Pasteur's dictum that chance favors the mind that is prepared; that is the importance of avoiding rigid adherence to fixed ideas. It is quite natural for the uninstructed intelligence to find a comfortable security and serenity in a set of conventional opinions which have been satisfactorily prearranged. The unusual is promptly dismissed because it is not wanted; it does not conform to the preconceived plan. The possibility of adventures in ideas is unknown to such benighted persons. We who live in a world which we recognize as not settled, stationary and finally immobilized, but as presenting all manner of possibilities of novel and unprecedented combinations and readjustments, must keep our minds open and recipient, ready for new views and fresh advances. We must not dismiss the unusual and the extraordinary aspects of experience as unworthy of attention; they may be the little beginnings of trails leading to great unexplored ranges of achievement. In a world organization which is in flux, in an anxious society groping its way possibly to new forms, shall we blind our eyes?

The great solutions may arrive unheralded, and unless we are prepared to weigh ideas on their merits and judge them fairly and critically we may not be participants in the momentous decisions, but, instead, worried and unhappy bystanders.

Regard for learning of the past, tolerance and free discussion of novel suggestions and readiness for cautious experimenting when opportunity offers—these features are typical of the prepared mind. They are typical, also, of the finest educational spirit. Indeed, it may be questioned whether a teacher who does not cherish an unprejudiced respect for the truth as handed down by our forebears and who is not on the alert for new revelations in the continuously opening vistas of truth—it may be questioned whether a teacher, lacking these fundamental attributes of intellectual integrity, is likely, himself, to develop minds which look out upon the world with perspicacity and adaptable understanding. A teacher is likely to create students in his own image. Alert and thoughtful graduates will go forth from a school or college when alert and thoughtful teachers, encouraged and fostered in their labors, exert their influence within its portals.

Here, I think, is a further implication of Pasteur's dictum that chance favors the prepared mind. That is that a school or college, by inspiring students with the high ideals of the best educational tradition, can make them ready to take advantage of the fortunate events which, amid extremely difficult and complex situations, are sure to appear. Not only in the physical and the biological sciences, from which I have drawn most of my illustrations, but to quite as great a degree in political, economic and social affairs, important and pressing problems call for solutions. A better world for all of us will be ours when these problems are solved. Many new discoveries are needed in order that these problems may be solved—discoveries of ways to achieve more perfect justice among men, a fairer distribution of the abundance which agriculture and industry can produce, assurance of conditions which will promote good health and effective medical care, freedom from the distress caused by great oscillations between financial booms and depressions, the reduction of crime and the number of criminals, the stabilization of family life, and the avoidance or rectification of numerous other social maladjustments. These are not hopeless situations. They can be largely remedied. The discoveries which will yield deeper insight into the modes of resolving these difficult and often baffling problems are likely to be made by minds which have been disciplined in directions which we have already considered. And when such minds confront the complexities involved in these extremely puzzling social and economic questions, they may be sure that quite unforeseen possibilities of securing answers will spring forth—chances of serendipity, for which they will be sagacious.